

CLAIMS

What is claimed is:

- 1 1. A method for diagnosis of a disorder associated with the development
2 of beta amyloid deposits or fibrils in a human or animal subject or assessing
3 the efficacy of treatment rendered to the subject for such disorder, said
4 method comprising the step of:
5 A) determining the presence of mtDNA CR mutations.
- 1 2. A method according to Claim 1, wherein Step A comprises making a
2 qualitative determination that mtDNS CR mutation is or is not present.
- 1 3. A method according to Claim 1, wherein Step A comprises making a
2 quantitative determination of mtDNS CR mutations.
- 1 4. A method according to Claim 3 further comprising the step of:
2 B) comparing a mtDNS CR value obtained by the quantitative
3 determination made in Step A with a control mtDNS CR value to determine
4 whether the subject has significantly more mtDNS CR mutations than control.
- 1 5. A method according to Claim 3 further comprising the step of:
2 B) comparing a mtDNS CR value obtained by the quantitative
3 determination made in Step A with a mtDNS CR value representative of
4 subjects who suffer from a disorder associated with the development of beta
5 amyloid deposits or fibrils.
- 1 6. A method according to any of Claim 1 wherein Step A comprises
2 testing for a T4141G mutation.
- 1 7. A method according to any of Claim 1 wherein Step A comprises
2 testing for a T414C mutation.

- 1 8. A method according to any of Claim 1 wherein Step A comprises
2 testing for a T477C mutation.
- 1 9. A method according to any of Claim 1 wherein Step A comprises
2 testing for a T146C mutation.
- 1 10. A method according to any of Claim 1 wherein Step A comprises
2 testing for a T152C mutation.
- 1 11. A method according to any of Claim 1 wherein Step A comprises
2 testing for a A189G mutation.
- 1 12. A method according to any of Claim 1 wherein Step A comprises
2 testing for a T195C mutation.
- 1 13. A method according to Claim 1 wherein Step A is carried out at least in
2 part by PNA-clamping PCR.
- 1 14. A method according to Claim 1 wherein Step A is carried out at least in
2 part by oligonucleotide hybridization.
- 1 15. A method according to Claim 1 wherein Step A is carried out at least in
2 part by primer extension.
- 1 16. A method according to Claim 1 wherein Step A is carried out at least in
2 part by restriction digestion.
- 1 17. A method according to Claim 1 wherein the determination of Step A is
2 made in a specimen of tissue, cells or body fluid selected from the group
3 consisting of:
4 i. brain tissue;
5 ii. brain tissue from the frontal cortex;
6 iii. nervous tissue;
7 iv. nerve cells

- 8 v. blood
- 9 vi. blood cells;
- 10 vii. urine;
- 11 viii. urinary tract cells;
- 12 ix. skin;
- 13 x. skin cells;
- 14 xi. epithelium;
- 15 xii. epithelial cells;
- 16 xiii. fibroblasts;
- 17 xiv. cerebrospinal fluid; and
- 18 xv. cells contained in cerebrospinal fluid.

1 18. A method according to Claim 1 wherein the method is carried out for
2 post-symptomatic diagnosis of a disorder in a subject who has begun to
3 exhibit symptoms of that disorder.

1 19. A method according to Claim 1 wherein the method is carried out for
2 pre-symptomatic diagnosis of a disorder in a subject who has not begun to
3 exhibit symptoms of that disorder.

1 20. A method according to Claim 1 wherein the disorder is a
2 neurodegenerative disease.

1 21. A method according to Claim 1 wherein the disorder is Alzheimer's
2 Disease.

1 22. A method according to Claim 1 wherein the disorder is Parkinson's
2 Disease.

1 23. A method according to Claim 1 wherein the disorder is Down's
2 Syndrome-associated dementia.

1 24. A method according to Claim 1 wherein the disorder is a spongiform
2 encephalopathy.

- 1 25. A method according to Claim 1 wherein the disorder is type II diabetes.
- 1 26. A method according to Claim 1 wherein the disorder is Creutzfeldt-
2 Jakob disease.
- 1 27. A method according to Claim 1 wherein the disorder is a Huntington's
2 disease.
- 1 28. A method according to Claim 1 wherein the disorder is macular
2 degeneration.
- 1 29. A method according to Claim 1 wherein the disorder is a prion disease.
- 1 30. A method according to Claim 1 wherein Step A comprises:
2 obtaining sample cells from the subject;
3 extracting DNA from the sample cells;
4 subjecting the extracted DNA to mitochondrial DNA control region
5 amplification;
6 determining whether homoplasmic 414 and 477 nucleotide variants are
7 present by direct sequencing for heteroplasmic 414 and 477 nucleotide
8 mutations; and
9 if 414 and 477 nucleotide variants are detected, cloning the mutant
10 molecules and sequencing the clone.
- 1 31. A test system comprising reagents and/or materials useable to perform
2 a method according to any of Claims 1-30.
- 1 32. A test system according to claim 31 further comprising instructions for
2 use.
- 1 33. A test system according to claim 31 further comprising a reference
2 containing control data.

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- 1 34. A test system according to claim 33 wherein the reference comprises
 - 2 computer software.